(FILE 'HOME' ENTERED AT 11:10:30 ON 08 SEP 2000)

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, USPATFULL' ENTERED AT 11:11:04 ON 08 SEP 2000

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L1       120898 S (CYTOKINE? OR INTERLEULIN? OR CHEMOKINE? OR LYMPHOKINE? OR
LY
L2         6489 S (?ASSAY? OR MEASUR? OR DETECT? OR DETERMIN?) (5A) L1
L3         6489 S L1 AND L2
L4         3796 S L1 (5A) ((IN VIVO) OR ENDOGEN?)
L5          346 S L4 AND L3
L6          154 DUP REM L5 (192 DUPLICATES REMOVED)
L7           20 S L2 (5A) (SANDWICH OR IMMUNOMETRIC)
L8            7 DUP REM L7 (13 DUPLICATES REMOVED)
                E FINKELMAN/IN
L9            2 S E5
                E MORRIS-S
                E MORRIS S/IN
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L8 ANSWER 2 OF 7 USPATFULL

ACCESSION NUMBER:	1999:124479 USPATFULL
TITLE:	Polypeptides and methods for the detection of L. tropica infection
INVENTOR(S):	Dillon, Davin C., Redmond, WA, United States Reed, Steven G., Bellevue, WA, United States
PATENT ASSIGNEE(S):	Corixa Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5965142	19991012	
APPLICATION INFO.:	US 1995-511872	19950804	(8)
DOCUMENT TYPE:	Utility		
PRIMARY EXAMINER:	Minnifield, Nita		
LEGAL REPRESENTATIVE:	Seed and Berry LLP		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	22 Drawing Figure(s); 10 Drawing Page(s)		
LINE COUNT:	1660		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 3 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 1

ACCESSION NUMBER:	1999105327 EMBASE
TITLE:	Newly synthesized phosphodiesterase 4 (PDE4) inhibitor, DWP205505, inhibits TNF-.alpha. secretion and mRNA expression.
AUTHOR:	Lee S.K.; Lee S.-A.; Byun H.; Cho M.-L.; Kim W.-U.; Park S.-H.; Cho C.-S.; Joo Y.-S.; Lee S.-S.; Yoo E.-S.; Ho Jung Son; Kim H.-Y.
CORPORATE SOURCE:	S.K. Lee, Research Institute of Immunobiology, Catholic Res. Inst. of Med. Sci., Catholic University of Korea, Seoul 157-701, Korea, Republic of. sukklee@cmc.cuk.ac.kr
SOURCE:	Journal of Microbiology and Biotechnology, (1999) 9/1 (106-112). Refs: 23 ISSN: 1017-7825 CODEN: JOMBES
COUNTRY:	Korea, Republic of
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	026 Immunology, Serology and Transplantation 031 Arthritis and Rheumatism 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English

L8 ANSWER 4 OF 7 MEDLINE DUPLICATE 2

ACCESSION NUMBER:	1998234052 MEDLINE
DOCUMENT NUMBER:	98234052
TITLE:	Production of proinflammatory cytokines and inflammatory mediators in human intestinal epithelial cells after invasion by Trichinella spiralis.
AUTHOR:	Li C K; Seth R; Gray T; Bayston R; Mahida Y R; Wakelin D
CORPORATE SOURCE:	Department of Life Science, University of Nottingham, United Kingdom.
SOURCE:	INFECTION AND IMMUNITY, (1998 May) 66 (5) 2200-6. Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY:	United States Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English

FILE SEGMENT: Cancer Journals; Priority Journals
ENTRY MONTH: 199807

L8 ANSWER 2 OF 7 USPATFULL
DETD **Cytokine production** of IFN-.gamma. was **measured** by a double **sandwich** ELISA using mouse anti-human IFN-8 Mab (Chemicon, Temucula, Calif.) and polyclonal rabbit anti-human IFN-8 serum. A standard curve was generated. . .

L8 ANSWER 3 OF 7 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 1
AB . . . DWP205505, on TNF-.alpha. and IL-10 production was tested in cells isolated from normal peripheral blood and rheumatoid arthritis synovial fluid. **Cytokine production** was **assayed** at the protein level by **sandwich** enzyme-linked immunosorbent assay (ELISA) and at the mRNA expression level by semi-quantitative RT-PCR. Another PDE4 inhibitor, RP73401, was used for. . .

L8 ANSWER 4 OF 7 MEDLINE DUPLICATE 2
AB . . . T. spiralis invasion. Increased levels of IL-8 were also released from the basolateral surfaces of infected monolayers as detected by **sandwich** enzyme-linked immunosorbent **assay**. Induction and **secretion** of proinflammatory **cytokines** in epithelial cells after nematode or bacterial invasion may initiate the acute inflammatory response of the small intestine. The upregulation. . .

L6 ANSWER 33 OF 154 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2000014655 MEDLINE
DOCUMENT NUMBER: 20014655
TITLE: Development of an **assay** to **measure** in **vivo cytokine production** in the mouse.
AUTHOR: Finkelman F D; Morris S C
CORPORATE SOURCE: Division of Immunology, University of Cincinnati College of Medicine, Cincinnati, OH 45267, USA.
CONTRACT NUMBER: RO1-AI35987 (NIAID)
RO1-AI37180 (NIAID)
SOURCE: INTERNATIONAL IMMUNOLOGY, (1999 Nov) 11 (11) 1811-8.
Journal code: AY5. ISSN: 0953-8178.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB The short in vivo lifespan of many cytokines can make **measurement** of in **vivo cytokine production** difficult. A method was developed to measure in vivo IL-4 and IFN-gamma production that eliminates this problem. Mice are injected with a biotin-labeled neutralizing IgG anti-IL-4 or anti-IFN-gamma mAb and bled 2-24 h later. **Secreted cytokine** is captured by the biotin-labeled mAb to produce a complex that has a relatively long in vivo half-life and consequently accumulates in serum. Serum concentrations of the complex are determined by ELISA, using wells coated with an antibody to a second epitope on the same cytokine to capture the complex. This technique is specific and increases sensitivity of detection of secreted IL-4 at least 1000-fold. The amount of cytokine measured is directly proportional to the amount produced and relatively independent of the site of **cytokine production**. Furthermore, because mice are injected with small quantities of biotin-labeled anti-cytokine mAb, which sample, rather than neutralize, all **secreted cytokines**, **cytokine** -dependent responses are not inhibited. The in vivo half-lives of the cytokine-anti-cytokine mAb complexes are sufficiently short to allow **cytokine production** to be **measured** every 2-3 days in the same mice. Thus, use of this assay provides a practical and relatively simple and inexpensive way to **measure** ongoing in **vivo cytokine production**. Furthermore, the techniques that have been developed to measure in vivo production of IL-4 and IFN-gamma can be applied to in vivo measurement of other molecules that have a short in vivo lifespan, including other cytokines.
TI Development of an **assay** to **measure** in **vivo cytokine production** in the mouse.
AB The short in vivo lifespan of many cytokines can make **measurement** of in **vivo cytokine production** difficult. A method was developed to measure in vivo IL-4 and IFN-gamma production that eliminates this problem. Mice are injected with a biotin-labeled neutralizing IgG anti-IL-4 or anti-IFN-gamma mAb and bled 2-24 h later. **Secreted cytokine** is captured by the biotin-labeled mAb to produce a complex that has a relatively long in vivo half-life and consequently. . . 1000-fold. The amount of cytokine measured is

directly proportional to the amount produced and relatively independent of the site of **cytokine production**. Furthermore, because mice are injected with small quantities of biotin-labeled anti-cytokine mAb, which sample, rather than neutralize, all **secreted cytokines**, **cytokine**-dependent responses are not inhibited. The in vivo half-lives of the cytokine-anti-cytokine mAb complexes are sufficiently short to allow **cytokine production** to be **measured** every 2-3 days in the same mice. Thus, use of this assay provides a practical and relatively simple and inexpensive way to **measure** ongoing in **vivo cytokine production**. Furthermore, the techniques that have been developed to measure in vivo production of IL-4 and IFN-gamma can be applied to. . .

L6 ANSWER 98 OF 154 MEDLINE DUPLICATE 36
ACCESSION NUMBER: 97158580 MEDLINE
DOCUMENT NUMBER: 97158580
TITLE: A comparison between ELISPOT methods for the **detection** of **cytokine producing** cells: greater sensitivity and specificity using ELISA plates as compared to nitrocellulose membranes.
AUTHOR: Ronnelid J; Klareskog L
CORPORATE SOURCE: Department of Rheumatology, Karolinska Hospital, Stockholm, Sweden.
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1997 Jan 15) 200 (1-2) 17-26.
Journal code: IFE. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199704
ENTRY WEEK: 19970403
AB We have used the ELISPOT method employing plastic ELISA plates without substrate in agar for the detection of single cells producing interferon-gamma (IFN-gamma) and interleukin-4 (IL-4). When using PBMC directly stimulated in the assay wells with T cell mitogens it was possible to measure production of human IFN-gamma at an earlier time point and with a higher sensitivity compared to conventional nitrocellulose plates. The plastic surface was not autostimulatory for IFN-gamma production, as seems to be the case for nitrocellulose surfaces. Compared to the use of nitrocellulose plates, the use of plastic ELISA plates is considerably cheaper and easier to perform. The increased sensitivity for cytokine detection, together with minimal autostimulatory properties of the detection surface, makes this method suitable for the **detection** of spontaneous low grade **cytokine production** from cells obtained in **vivo**.
TI A comparison between ELISPOT methods for the **detection** of **cytokine producing** cells: greater sensitivity and specificity using ELISA plates as compared to nitrocellulose membranes.
AB . . . increased sensitivity for cytokine detection, together with minimal autostimulatory properties of the detection surface, makes this method suitable for the **detection** of spontaneous low grade **cytokine production** from cells obtained in **vivo**
.

L6 ANSWER 150 OF 154 MEDLINE DUPLICATE 77
ACCESSION NUMBER: 89327952 MEDLINE
DOCUMENT NUMBER: 89327952
TITLE: In vitro **detection** of **lymphokines produced** by in **vivo** activated lymphocytes.
AUTHOR: Mohler K M; Butler L D
CORPORATE SOURCE: Department of Immunology, Lilly Research Laboratories, Corporate Center, Indianapolis, IN 46285..
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1989 Jul 6) 121 (1) 67-73.
Journal code: IFE. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198911
AB The purpose of these experiments was to develop a method to **measure** the **production** of **lymphokines** by cells which were activated by antigen in vivo. Previous protocols have been relatively unsuccessful since small, if any, amounts of lymphokines were available for measurement when in vivo antigen activated lymphocytes (AAL) were examined. These unsuccessful experiments usually employed supernatants derived from in vivo AAL which had been cultured in vitro for 4-24 h. As an alternative to assaying supernatants for the presence/absence of lymphokines, we have developed a co-culture system in which the indicator cells are directly added to the wells containing the in vivo AAL. Utilizing this system in conjunction with appropriate neutralizing monoclonal antibodies, we have demonstrated that interleukin-2, interleukin-3/colony stimulating factor and tumor necrosis factor-alpha can be readily detected from in vivo AAL.
TI In vitro **detection** of **lymphokines produced** by in **vivo** activated lymphocytes.
AB The purpose of these experiments was to develop a method to **measure** the **production** of **lymphokines** by cells which were activated by antigen in vivo. Previous protocols have been relatively unsuccessful since small, if any, amounts. . .

L6 ANSWER 123 OF 154 MEDLINE
ACCESSION NUMBER: 95019210 MEDLINE
DOCUMENT NUMBER: 95019210
TITLE: Development of immunoassay for cytokines and its clinical significance.
AUTHOR: Ohmoto Y
CORPORATE SOURCE: Cellular Technology Institute, Otsuka Pharmaceutical Co. Ltd., Tokushima..
SOURCE: RINSHO BYORI. JAPANESE JOURNAL OF CLINICAL PATHOLOGY, (1994 Aug) 42 (8) 825-33. Ref: 26
Journal code: KIV. ISSN: 0047-1860.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
ENTRY MONTH: 199501

AB As measurement systems of cytokines have recently been developed, there are many reports indicating the relationship between cytokines and various diseases. We have also developed various new measurement systems using gene technology and hybridoma technology. The measurement system is composed of the following 5 steps. (1) Cloning of cytokines, (2) Expression of cytokines, (3) Purification of cytokines, (4) Preparation of antibodies (monoclonal and polyclonal antibodies), (5) Development of immunoassay. Cytokines are measured not only in the cytokine itself but also in the receptor, receptor antagonist, and autoantibody. We established the measurement system of cytokines using ELISA (antibody is labeled by enzyme.) for the cytokine itself and RIA (antigen is labeled by isotope.) for the autoantibody to cytokines. The blood concentration of cytokines is low because **cytokines** are utilized immediately after **production** and excreted into the urine. Therefore, the immunological responses of individuals can be determined by an ex **vivo measurement** of the **production** of **cytokines** by stimulation of whole blood with LPS not by simply measuring the cytokine itself in plasma. We call this method "Whole Blood Induction Method". This method is positioned as one of the methods which shows the immunological response of cytokines to the outer body at the time of infection using a low volume of human blood. Finally, studies of cytokines have been carried out not only in immunological systems but also in hormone systems which are closely related to cytokines. Studies have also expanded to fields which, to date, have not been thought to be related by investigating adherence factors.(ABSTRACT TRUNCATED AT 250 WORDS)

AB . . . and RIA (antigen is labeled by isotope.) for the autoantibody to cytokines. The blood concentration of cytokines is low because **cytokines** are utilized immediately after **production** and excreted into the urine. Therefore, the immunological responses of individuals can be determined by an ex **vivo measurement** of the **production** of **cytokines** by stimulation of whole blood with LPS not by simply measuring the cytokine itself in plasma. We call this method. . .

L6 ANSWER 151 OF 154 MEDLINE
TI Cytokines in radioprotection. Comparison of the radioprotective effects of
IL-1 to IL-2, GM-CSF and IFN gamma.

L6 ANSWER 152 OF 154 MEDLINE DUPLICATE 78
TI Identification of beta-lymphotoxin as the predominant molecular class of in vitro and in vivo Syrian hamster lymphotoxin.

L6 ANSWER 153 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI Serum leukocyte inhibitory factor in cancer patients (serum LIF).

L6 ANSWER 154 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI [Phytohemagglutinin induced lymphotoxin formation and lymphocytic blast transformation in children with immunologic deficiencies]. PHYTOHAMAGGLUTININ INDUZIERTE LYMPHOTOXIN BILDUNG UND LYMPHOZYTEN BLASTENTRANSFORMATION BEI KINDERN MIT IMMUNDEFEKTEN.

=> d l6 ti 1-154

L6 ANSWER 1 OF 154 USPATFULL
TI Aminoalkyl glucosamine phosphate compounds and their use as adjuvants and immunoeffectors

L6 ANSWER 2 OF 154 USPATFULL
TI Recombinant expression of proteins from secretory cell lines

L6 ANSWER 3 OF 154 USPATFULL
TI Process of making tosylbenzyl formamide derivatives

L6 ANSWER 4 OF 154 USPATFULL
TI Pyrimidine compounds useful in treating cytokine mediated diseases

L6 ANSWER 5 OF 154 USPATFULL
TI Method of converting a Th2-type allergic immune response into a Th1-type immune response

L6 ANSWER 6 OF 154 USPATFULL
TI Diagnosis, prevention and treatment of ulcerative colitis, and clinical subtypes thereof, using histone H1

L6 ANSWER 7 OF 154 USPATFULL
TI Interleukin-12 as an adjuvant for paramyxoviridae vaccines

L6 ANSWER 8 OF 154 USPATFULL
TI Rapid production of autologous tumor vaccines

L6 ANSWER 9 OF 154 USPATFULL
TI Method and assay for regulation of T cell proliferation

L6 ANSWER 10 OF 154 USPATFULL
TI Diagnosis, prevention and treatment of ulcerative colitis, and clinical subtypes thereof, using microbial UC pANCA antigens

L6 ANSWER 11 OF 154 USPATFULL
TI Method of using tetracycline compounds to enhance interleukin-10

production

L6 ANSWER 12 OF 154 USPATFULL
TI Use of estrone derivatives as steroid sulphatase inhibitors

L6 ANSWER 13 OF 154 MEDLINE DUPLICATE 1
TI Cardiopulmonary bypass decreases **cytokine production** in lipopolysaccharide-stimulated whole blood cells: roles of interleukin-10 and the extracorporeal circuit.

L6 ANSWER 14 OF 154 MEDLINE DUPLICATE 2
TI Reduced Th1, but not Th2, **cytokine production** by lymphocytes after in **vivo** exposure of healthy subjects to endotoxin.

L6 ANSWER 15 OF 154 MEDLINE DUPLICATE 3
TI **Measurement** of in **vivo** rectal mucosal **cytokine** and eicosanoid **production** in ulcerative colitis using filter paper.

L6 ANSWER 16 OF 154 MEDLINE DUPLICATE 4
TI Encapsulated fish oil enriched in alpha-tocopherol alters plasma phospholipid and mononuclear cell fatty acid compositions but not mononuclear cell functions.

L6 ANSWER 17 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 5
TI The interaction between cytokines and neurotransmitters in depression and stress: Possible mechanism of antidepressant treatments.

L6 ANSWER 18 OF 154 MEDLINE DUPLICATE 6
TI In vitro and in vivo immunostimulatory potential of bone marrow-derived mast cells on B- and T-lymphocyte activation.

L6 ANSWER 19 OF 154 USPATFULL
TI Polynucleotides encoding myeloid progenitor inhibitory factor-1 (MPIF-1)
and polypeptides encoded thereby

L6 ANSWER 20 OF 154 USPATFULL
TI Substituted imidazole compounds

L6 ANSWER 21 OF 154 USPATFULL
TI Amide compounds

L6 ANSWER 22 OF 154 USPATFULL
TI Method for measuring endogenous cytokines

L6 ANSWER 23 OF 154 USPATFULL
TI Screening methods for cytokine inhibitors

L6 ANSWER 24 OF 154 USPATFULL
TI Gene therapy for effector cell regulation

L6 ANSWER 25 OF 154 USPATFULL
TI Cycloalkyl substituted imidazoles

L6 ANSWER 26 OF 154 USPATFULL
TI Methods for augmenting immunological responses through the administration of dehydroepiandrosterone (DHEA) and dehydroepiandrosterone-sulfate (DHEA-S)

L6 ANSWER 27 OF 154 USPATFULL
TI Pyrimidinyl imidazoles

L6 ANSWER 28 OF 154 USPATFULL
TI Process of preparing imidazole compounds

L6 ANSWER 29 OF 154 USPATFULL
TI Substituted imidazole compounds

L6 ANSWER 30 OF 154 USPATFULL
TI Therapeutic uses of bactericidal/permeability-increasing protein dimer products

L6 ANSWER 31 OF 154 MEDLINE DUPLICATE 7
TI POMC gene-derived peptides activate melanocortin type 3 receptor on murine
macrophages, suppress **cytokine release**, and inhibit
neutrophil migration in acute experimental inflammation.

L6 ANSWER 32 OF 154 MEDLINE DUPLICATE 8
TI Neutralization of endogenous granulocyte-macrophage colony-stimulating factor subverts the protective immune response to Histoplasma capsulatum.

L6 ANSWER 33 OF 154 MEDLINE DUPLICATE 9
TI Development of an **assay** to **measure** in **vivo**
cytokine production in the mouse.

L6 ANSWER 34 OF 154 MEDLINE DUPLICATE 10
TI Acadesine during fluid resuscitation from shock and abdominal sepsis [see comments].

L6 ANSWER 35 OF 154 MEDLINE DUPLICATE 11
TI Differential effect of anti-TNF-alpha antibody on proinflammatory
cytokine release by Kupffer cells following liver
ischemia and reperfusion.

L6 ANSWER 36 OF 154 MEDLINE DUPLICATE 12
TI The mechanism of activation of NK-cell IFN-gamma production by ligation of
CD28.

L6 ANSWER 37 OF 154 MEDLINE DUPLICATE 13
TI Priming of **cytokine release** and increased levels of
bactericidal permeability-increasing protein in the blood of animal facility workers.

L6 ANSWER 38 OF 154 MEDLINE DUPLICATE 14
TI [Prophylactic effectiveness of propolis for immunostimulation: a clinical pilot study].
Prophylaktische Wirkungen von Propolis zur Immunstimulation: Eine klinische Pilotstudie.

L6 ANSWER 39 OF 154 MEDLINE DUPLICATE 15
TI Effects of modulating TGF-beta 1 on immune responses to mycobacterial infection in guinea pigs.

L6 ANSWER 40 OF 154 BIOSIS COPYRIGHT 2000 BIOSIS
TI In vivo sensitivity of human melanoma to tumor necrosis factor (TNF)-alpha
is **determined** by tumor **production** of the novel
cytokine endothelial-monocyte activating polypeptide II (EMAPII.

L6 ANSWER 41 OF 154 MEDLINE
TI The development of non-animal-based bioassays for cytokines and growth factors.

L6 ANSWER 42 OF 154 MEDLINE DUPLICATE 16
TI Ex vivo effects of lactobacilli, streptococci, and bifidobacteria
ingestion on **cytokine** and nitric oxide **production** in a
murine model.

L6 ANSWER 43 OF 154 MEDLINE DUPLICATE 17
TI Disease-specific ex **vivo** stimulation of whole blood for **cytokine production**: applications in the study of tuberculosis.

L6 ANSWER 44 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 18
TI [Hemodialysis-associated induction of cytokines]. ZYTOKININDUKTION WAHREND DER HAMODIALYSE: MECHANISMEN UND KLINISCHE RELEVANZ.

L6 ANSWER 45 OF 154 MEDLINE DUPLICATE 19
TI Heterozygous defect in HIV-1 coreceptor CCR5 and **chemokine production**.

L6 ANSWER 46 OF 154 USPATFULL
TI Process of preparing imidazole compounds

L6 ANSWER 47 OF 154 USPATFULL
TI Pharmaceutical dipeptide compositions and methods of use thereof: immunodepressants

L6 ANSWER 48 OF 154 USPATFULL
TI Naphthyridinone derivatives

L6 ANSWER 49 OF 154 USPATFULL
TI Use of interleukin-10 analogs for antagonists to treat endotoxin- or superantigen-induced toxicity

L6 ANSWER 50 OF 154 USPATFULL
TI Use of an interleukin-10 antagonist to treat a B cell mediated autoimmune disorder

L6 ANSWER 51 OF 154 USPATFULL
TI Use of interleukin-10 (IL-10) to treat endotoxin- or superantigen-induced toxicity

L6 ANSWER 52 OF 154 USPATFULL
TI Peptides with bactericidal activity and endotoxin neutralizing activity for gram negative bacteria and methods for their use

L6 ANSWER 53 OF 154 USPATFULL
TI T-cell receptors and their use in therapeutic and diagnostic methods

L6 ANSWER 54 OF 154 USPATFULL
TI Recombinant mycobacterial vaccines

L6 ANSWER 55 OF 154 USPATFULL
TI Method for enhancement of **production** of **lymphokines** and applications thereof

L6 ANSWER 56 OF 154 USPATFULL
TI TNF-.alpha. ribozymes

L6 ANSWER 57 OF 154 USPATFULL
TI Method for treatment of purulent inflammatory diseases

L6 ANSWER 58 OF 154 USPATFULL
TI Recombinant mycobacterial vaccines

L6 ANSWER 59 OF 154 USPATFULL
TI Use of interleukin-10 in adoptive immunotherapy of cancer

L6 ANSWER 60 OF 154 USPATFULL
TI Methods for measurement of lymphocyte function

L6 ANSWER 61 OF 154 USPATFULL
TI Pharmaceutical dipeptide compositions and methods of use thereof: systemic toxicity

L6 ANSWER 62 OF 154 USPATFULL
TI Substituted imidazole compounds

L6 ANSWER 63 OF 154 USPATFULL
TI Method for augmenting immunological responses

L6 ANSWER 64 OF 154 USPATFULL
TI Yolk sac stem cells and their uses

L6 ANSWER 65 OF 154 USPATFULL
TI Imidazole compounds and compositions

L6 ANSWER 66 OF 154 USPATFULL
TI Hematopoietic cells: compositions and methods

L6 ANSWER 67 OF 154 USPATFULL
TI Methods for normalizing numbers of lymphocytes

L6 ANSWER 68 OF 154 USPATFULL
TI Substituted imidazole compounds

L6 ANSWER 69 OF 154 USPATFULL
TI Naphthyridine derivatives

L6 ANSWER 70 OF 154 MEDLINE DUPLICATE 20
TI Expansion of Philadelphia chromosome-negative CD3(+)CD56(+) cytotoxic cells from chronic myeloid leukemia patients: in vitro and in vivo efficacy in severe combined immunodeficiency disease mice.

L6 ANSWER 71 OF 154 MEDLINE DUPLICATE 21
TI Diltiazem modulates monokine production in human mixed lymphocyte culture.

L6 ANSWER 72 OF 154 BIOSIS COPYRIGHT 2000 BIOSIS
TI Effect of bronchial allergen challenge on in vitro **cytokine release** by peripheral blood mononuclear cells of atopic patients.

L6 ANSWER 73 OF 154 MEDLINE DUPLICATE 22
TI Effect of bronchial allergen challenge on in vitro **cytokine release** by peripheral blood mononuclear cells of atopic patients.

L6 ANSWER 74 OF 154 MEDLINE DUPLICATE 23
TI Transmembrane polar residues of TCR beta chain are required for signal transduction.

L6 ANSWER 75 OF 154 MEDLINE DUPLICATE 24
TI Filgrastim restores interleukin-2 production in blood from patients with advanced human immunodeficiency virus infection.

L6 ANSWER 76 OF 154 MEDLINE DUPLICATE 25
TI Impaired production of IL-12 in system lupus erythematosus. II: IL-12 production in vitro is correlated negatively with serum IL-10, positively with serum IFN-gamma and negatively with disease activity in SLE.

L6 ANSWER 77 OF 154 MEDLINE DUPLICATE 26
TI Effects of clozapine on in vitro immune parameters: a longitudinal study in clozapine-treated schizophrenic patients.

L6 ANSWER 78 OF 154 MEDLINE DUPLICATE 27
TI Determination of tumour necrosis factor-alpha and interleukin-10 production in a whole blood stimulation system: assessment of laboratory error and individual variation.

L6 ANSWER 79 OF 154 BIOSIS COPYRIGHT 2000 BIOSIS
TI Determination of tumour necrosis factor-alpha and interleukin-10 production in a whole blood stimulation system: Assessment of laboratory error and individual variation.

L6 ANSWER 80 OF 154 MEDLINE DUPLICATE 28
TI Proinflammatory cytokine gene expression in whole blood from patients undergoing coronary artery bypass surgery and its modulation by pentoxifylline.

L6 ANSWER 81 OF 154 USPATFULL
TI Therapeutic uses of bactericidal-permeability-increasing protein dimer products

L6 ANSWER 82 OF 154 USPATFULL
TI Pyridyl imidazole compounds and compositions

L6 ANSWER 83 OF 154 USPATFULL
TI Process for preparing pyrimidyl imidazoles

L6 ANSWER 84 OF 154 USPATFULL
TI Imidazole compounds, compositions and use

L6 ANSWER 85 OF 154 USPATFULL
TI Method of refolding human IL-13

L6 ANSWER 86 OF 154 USPATFULL
TI Compounds

L6 ANSWER 87 OF 154 USPATFULL
TI Imidazole compounds, use and process of making

L6 ANSWER 88 OF 154 USPATFULL
TI Recombinant BCG

L6 ANSWER 89 OF 154 MEDLINE DUPLICATE 29
TI Pyridinyl imidazole inhibitors of p38 mitogen-activated protein kinase bind in the ATP site.

L6 ANSWER 90 OF 154 MEDLINE DUPLICATE 30
TI Characteristic T helper 2 T cell cytokine abnormalities in autoimmune lymphoproliferative syndrome, a syndrome marked by defective apoptosis and humoral autoimmunity.

L6 ANSWER 91 OF 154 MEDLINE DUPLICATE 31
TI Are CD8+ dendritic cells (DC) veto cells? The role of CD8 on DC in DC development and in the regulation of CD4 and CD8 T cell responses.

L6 ANSWER 92 OF 154 MEDLINE DUPLICATE 32
TI Pro- and anti-inflammatory cytokines in healthy volunteers fed various doses of fish oil for 1 year.

L6 ANSWER 93 OF 154 MEDLINE
TI Type 1 versus type 2 **cytokine release** by Vbeta T cell subpopulations **determines** in vivo antitumor reactivity: IL-10 mediates a suppressive role.

L6 ANSWER 94 OF 154 MEDLINE DUPLICATE 33
TI **Tumor** necrosis **factor** alpha and interleukin 6 **release** induced by antibiotic killing of Pseudomonas aeruginosa and Staphylococcus aureus.

L6 ANSWER 95 OF 154 MEDLINE DUPLICATE 34
TI "PERFEXT": a direct method for quantitative assessment of **cytokine**

production in **vivo** at the local level.

L6 ANSWER 96 OF 154 MEDLINE DUPLICATE 35
TI Role of polymorphic Fc receptor Fc gammaRIIa in **cytokine release** and adverse effects of murine IgG1 anti-CD3/T cell receptor antibody (WT31).

L6 ANSWER 97 OF 154 BIOSIS COPYRIGHT 2000 BIOSIS
TI Differentiation of naive human CD4 T cells into TH2/TH1 effectors.

L6 ANSWER 98 OF 154 MEDLINE DUPLICATE 36
TI A comparison between ELISPOT methods for the **detection** of **cytokine producing** cells: greater sensitivity and specificity using ELISA plates as compared to nitrocellulose membranes.

L6 ANSWER 99 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 37
TI Regulated **production** of **cytokines** in neutrophils.

L6 ANSWER 100 OF 154 USPATFULL
TI Method and kit for measuring endogenous cytokines

L6 ANSWER 101 OF 154 USPATFULL
TI Therapeutic, IL-6 antibody kits, and process for their preparation

L6 ANSWER 102 OF 154 USPATFULL
TI Method for enhancement of **production** of **lymphokines** and applications thereof

L6 ANSWER 103 OF 154 MEDLINE DUPLICATE 38
TI Nucleotide-free diet suppresses antigen-driven **cytokine production** by primed T cells: effects of supplemental nucleotides and dietary fatty acids.

L6 ANSWER 104 OF 154 MEDLINE DUPLICATE 39
TI Lymphocyte subsets, apoptosis, and cytokines in patients with chronic fatigue syndrome.

L6 ANSWER 105 OF 154 MEDLINE DUPLICATE 40
TI Features of the **cytokines secreted** by adult T cell leukemia (ATL) cells.

L6 ANSWER 106 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI Cytokines: Mediators of the inflammatory response to surgery.

L6 ANSWER 107 OF 154 MEDLINE DUPLICATE 41
TI Enhanced nasal **cytokine production** in human beings after in **vivo** challenge with diesel exhaust particles.

L6 ANSWER 108 OF 154 MEDLINE DUPLICATE 42
TI Direct measurement of cytokines (IFN-gamma, IL-4, -5, and -6) from organs after antigenic challenge.

L6 ANSWER 109 OF 154 MEDLINE DUPLICATE 43
TI Effects of in vitro hyperthermia on proliferative responses and lymphocyte activity.

L6 ANSWER 110 OF 154 USPATFULL
TI Therapeutic uses of bactericidal/permeability-increasing protein dimer products

L6 ANSWER 111 OF 154 MEDLINE DUPLICATE 44
TI Methylcholanthrene-induced mouse sarcomas express individually distinct major histocompatibility complex class I-associated peptides recognized by specific CD8+ T-cell lines.

L6 ANSWER 112 OF 154 MEDLINE DUPLICATE 45
TI Cytokine modulation alters pulmonary clearance of Rhodococcus equi and development of granulomatous pneumonia.

L6 ANSWER 113 OF 154 MEDLINE DUPLICATE 46
TI Effect of granulocyte colony-stimulating factor treatment on ex vivo blood cytokine response in human volunteers.

L6 ANSWER 114 OF 154 MEDLINE DUPLICATE 47
TI Neutralization of IL-10 increases lethality in endotoxemia. Cooperative effects of macrophage inflammatory protein-2 and tumor necrosis factor.

L6 ANSWER 115 OF 154 MEDLINE DUPLICATE 48
TI Effect of methotrexate alone or in combination with sulphasalazine on the **production** and circulating concentrations of **cytokines** and their antagonists. Longitudinal evaluation in patients with rheumatoid arthritis.

L6 ANSWER 116 OF 154 MEDLINE DUPLICATE 49
TI **Cytokine production** by mononuclear cells following stimulation with a peptide-containing, endotoxin-free Escherichia coli extract.

L6 ANSWER 117 OF 154 MEDLINE DUPLICATE 50
TI **Cytokine**-induced neutrophil chemoattractant **production** by primary rat alveolar type II cells.

L6 ANSWER 118 OF 154 MEDLINE DUPLICATE 51
TI Ex-**vivo** whole blood cultures for predicting **cytokine-release** syndrome: dependence on target antigen and antibody isotype.

L6 ANSWER 119 OF 154 USPATFULL
TI Class I MHC-restricted T-T hybridomas, and a CD8-transfected BW5147, fusion partner therefor

L6 ANSWER 120 OF 154 MEDLINE DUPLICATE 52
TI Different kinetic patterns of cytokine gene expression in vivo in orally tolerant mice.

L6 ANSWER 121 OF 154 MEDLINE DUPLICATE 53
TI Rapid establishment of a stable IL-4/IFN-gamma production profile in the antigen-specific CD4+ T cell response to protein immunization.

L6 ANSWER 122 OF 154 MEDLINE DUPLICATE 54
TI In **vivo cytokine production** and recombinant interleukin 2 immunotherapy: an insight into the possible mechanisms underlying clinical responses.

L6 ANSWER 123 OF 154 MEDLINE
TI Development of immunoassay for cytokines and its clinical significance.

L6 ANSWER 124 OF 154 MEDLINE DUPLICATE 55
TI Mice transgenic for a soluble form of murine CTLA-4 show enhanced expansion of antigen-specific CD4+ T cells and defective antibody production in vivo.

L6 ANSWER 125 OF 154 MEDLINE DUPLICATE 56
TI Acquisition of **lymphokine-producing** phenotype by CD4+ T cells.

L6 ANSWER 126 OF 154 MEDLINE DUPLICATE 57
TI T cell clones from psoriasis skin lesions can promote keratinocyte

proliferation in vitro via secreted products.

L6 ANSWER 127 OF 154 MEDLINE DUPLICATE 58
TI Individual cells simultaneously produce both IL-4 and IL-6 in vivo.

L6 ANSWER 128 OF 154 MEDLINE DUPLICATE 59
TI Concomitant in **vivo production** of 19 different **cytokines** in human tonsils.

L6 ANSWER 129 OF 154 MEDLINE DUPLICATE 60
TI High amounts of circulating interleukin (IL)-6 in the form of monomeric immune complexes during anti-IL-6 therapy. Towards a new methodology for **measuring** overall **cytokine production** in human in **vivo**.

L6 ANSWER 130 OF 154 MEDLINE DUPLICATE 61
TI **Determination** of **cytokine release** after in **vivo** and in vitro administration of Deodan (a preparation from Lactobacillus bulgaricus "LB51") by the rabbit pyrogen test.

L6 ANSWER 131 OF 154 MEDLINE
TI Studies on the **production** of **endogenous cytokines** in patients with renal cell carcinoma.

L6 ANSWER 132 OF 154 MEDLINE DUPLICATE 62
TI Circulating cytokine levels in patients with rheumatoid arthritis: results of a double blind trial with sulphasalazine.

L6 ANSWER 133 OF 154 MEDLINE DUPLICATE 63
TI Differential effects of cyclosporine and etretinate on serum cytokine levels in patients with psoriasis.

L6 ANSWER 134 OF 154 MEDLINE DUPLICATE 64
TI A polymerase chain reaction assay for the detection and quantitation of cytokine gene expression in small numbers of cells.

L6 ANSWER 135 OF 154 MEDLINE DUPLICATE 65
TI Tumor necrosis factor expression by human ovarian carcinoma in vivo.

L6 ANSWER 136 OF 154 MEDLINE DUPLICATE 66
TI Analysis of the time course of IFN-gamma mRNA and protein production during primary murine listeriosis. The immune phase of bacterial elimination is not temporally linked to IFN production in vivo.

L6 ANSWER 137 OF 154 MEDLINE DUPLICATE 67
TI **Release** of the **cytokines** colony-stimulating factor-1, granulocyte-macrophage colony-stimulating factor, and IL-6 by cloned murine vascular smooth muscle cells.

L6 ANSWER 138 OF 154 MEDLINE DUPLICATE 68
TI Ligand stimulation of transfected and **endogenous** growth factor receptors enhances **cytokine production** by mast cells.

L6 ANSWER 139 OF 154 MEDLINE DUPLICATE 69
TI Dissociation between plasma and monocyte-associated cytokines during sepsis.

L6 ANSWER 140 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 70
TI The role of lymphokines and cytokines in mucosal immune function.

L6 ANSWER 141 OF 154 MEDLINE DUPLICATE 71
TI Identification of cytokines which enhance (CSF-1, IL-3) or restrict (IFN-gamma) growth of intramacrophage Listeria monocytogenes.

L6 ANSWER 142 OF 154 MEDLINE DUPLICATE 72

TI Generation of cytokines in human visceral leishmaniasis: dissociation of endogenous TNF-alpha and IL-1 beta production.

L6 ANSWER 143 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI [Analytical, immunological and animal testing conditions for clinical tests of lectin contents in standardized mistletoe therapy]. ANALYTISCHE, IMMUNOLOGISCHE UND TIEREXPERIMENTELLE VORAUSSETZUNGEN FUR DIE KLINISCHE PRUFUNG DER AUF LEKTINGEHALT STANDARDISIERTEN MISTELTHERAPIE.

L6 ANSWER 144 OF 154 MEDLINE DUPLICATE 73
TI Frequency analysis of **lymphokine-secreting** CD4+ and CD8+ T cells activated in a graft-versus-host reaction.

L6 ANSWER 145 OF 154 SCISEARCH COPYRIGHT 2000 ISI (R)
TI OVERLOAD OF LUNG CLEARANCE IS ASSOCIATED WITH ACTIVATION OF ALVEOLAR MACROPHAGE **TUMOR**-NECROSIS-**FACTOR** AND FIBRONECTIN **RELEASE**

L6 ANSWER 146 OF 154 BIOSIS COPYRIGHT 2000 BIOSIS
TI LYMPHOKINE OVERPRODUCTION IN SEVERE APLASTIC ANEMIA IS NOT RELATED TO BLOOD TRANSFUSIONS.

L6 ANSWER 147 OF 154 MEDLINE DUPLICATE 74
TI MHC control of CD4+ T cell subset activation.

L6 ANSWER 148 OF 154 MEDLINE DUPLICATE 75
TI Regulation of murine **lymphokine production** in **vivo**. Ultraviolet radiation exposure depresses IL-2 and enhances IL-4 production by T cells through an IL-1-dependent mechanism.

L6 ANSWER 149 OF 154 MEDLINE DUPLICATE 76
TI Cell-mediated immunity to chemically xenogenized tumors--IV. **Production** of **lymphokine** activity by, and in response to, highly immunogenic cells.

L6 ANSWER 150 OF 154 MEDLINE DUPLICATE 77
TI In vitro **detection** of **lymphokines produced** by in **vivo** activated lymphocytes.

L6 ANSWER 151 OF 154 MEDLINE
TI Cytokines in radioprotection. Comparison of the radioprotective effects of IL-1 to IL-2, GM-CSF and IFN gamma.

L6 ANSWER 152 OF 154 MEDLINE DUPLICATE 78
TI Identification of beta-lymphotoxin as the predominant molecular class of in vitro and in vivo Syrian hamster lymphotoxin.

L6 ANSWER 153 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI Serum leukocyte inhibitory factor in cancer patients (serum LIF).

L6 ANSWER 154 OF 154 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
TI [Phytohemagglutinin induced lymphotoxin formation and lymphocytic blast transformation in children with immunologic deficiencies]. PHYTOHAMAGGLUTININ INDUZIERTE LYMPHOTOXIN BILDUNG UND LYMPHOZYTEN BLASTENTRANSFORMATION BEI KINDERN MIT IMMUNDEFEKTEN.

=> d his

(FILE 'HOME' ENTERED AT 11:10:30 ON 08 SEP 2000)

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, USPATFULL' ENTERED AT 11:11:04 ON 08 SEP 2000

L1	120898	S (CYTOKINE? OR INTERLEULIN? OR CHEMOKINE? OR LYMPHOKINE? OR LY
L2	6489	S (?ASSAY? OR MEASUR? OR DETECT? OR DETERMIN?) (5A) L1
L3	6489	S L1 AND L2
L4	3796	S L1 (5A) ((IN VIVO) OR ENDOGEN?)
L5	346	S L4 AND L3
L6	154	DUP REM L5 (192 DUPLICATES REMOVED)
L7	20	S L2 (5A) (SANDWICH OR IMMUNOMETRIC)
L8	7	DUP REM L7 (13 DUPLICATES REMOVED)

L9 ANSWER 1 OF 2 USPATFULL
ACCESSION NUMBER: 2000:61188 USPATFULL
TITLE: Pharmaceutical compositions comprising a soluble interleukin-4 receptor
INVENTOR(S): Maliszewski, Charles R., Seattle, WA, United States
Finkelman, Fred D., Rockville, MD, United States
PATENT ASSIGNEE(S): Immunex Corporation, Seattle, WA, United States (U.S. corporation)
The United States of America as represented by the Secretary of the Army, Washington, DC, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6063371	20000516
APPLICATION INFO.:	US 1996-714617	19960916 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-425308, filed on 17 Apr 1995, now abandoned which is a continuation of Ser.
No. US 1993-33874, filed on 19 Mar 1993, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Mertz, Prema
LEGAL REPRESENTATIVE: Seed and Bery, LLP; Anderson, Kathryn A.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 549
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The biological activity of exogenous ligand proteins is enhanced by intravenously co-administering to a mammal the ligand and a soluble receptor protein that binds thereto. Pharmaceutical compositions comprising a ligand protein complexed with a soluble receptor protein are provided. In certain embodiments, the ligand is selected from the group consisting of interleukins, colony stimulating factors, and tumor necrosis factor.

=> d l9 clm

L9 ANSWER 1 OF 2 USPATFULL
CLM What is claimed is:

1. A method of enhancing a biological activity of interleukin-4 (IL-4) in vivo, comprising intravenously co-administering to a mammal IL-4 and a soluble IL-4 receptor (sIL-4R), wherein the mammal is afflicted with a condition for which enhancement of the biological activity of the IL-4 is desired, and wherein the sIL-4R and IL-4 are co-administered in a molar ratio ranging from 30:1 to 1:1.

2. A method according to claim 1, wherein the sIL-4R and IL-4 are co-administered in a molar ratio ranging from 5:1 to 1:1.

3. The method according to any one of claims 1, or 2 wherein said sIL-4R and IL-4 are human sIL-4R and human IL-4.

4. A pharmaceutical composition comprising interleukin-4 (IL-4) and a soluble IL-4 receptor (sIL-4R), wherein the composition comprises sIL-4R and IL-4 in a molar ratio ranging from 30:1 to 1:1.

5. A pharmaceutical composition according to claim 4, wherein the composition comprises sIL-4R and IL-4 in a molar ratio ranging from 5:1 to 1:1.

6. The pharmaceutical composition according to any one of claim 4 or 5 wherein said sIL-4R and IL-4 are human sIL-4R and human IL-4.

L9 ANSWER 1 OF 2 USPATFULL

ACCESSION NUMBER: 2000:61188 USPATFULL

TITLE: Pharmaceutical compositions comprising a soluble interleukin-4 receptor

INVENTOR(S): Maliszewski, Charles R., Seattle, WA, United States
Finkelman, Fred D., Rockville, MD, United States

PATENT ASSIGNEE(S): Immunex Corporation, Seattle, WA, United States (U.S. corporation)
The United States of America as represented by the Secretary of the Army, Washington, DC, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6063371	20000516
APPLICATION INFO.:	US 1996-714617	19960916 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-425308, filed on 17 Apr 1995, now abandoned which is a continuation of Ser.
No. US 1993-33874, filed on 19 Mar 1993, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Mertz, Prema

LEGAL REPRESENTATIVE: Seed and Bery, LLP; Anderson, Kathryn A.

NUMBER OF CLAIMS: 6

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 549

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The biological activity of exogenous ligand proteins is enhanced by intravenously co-administering to a mammal the ligand and a soluble receptor protein that binds thereto. Pharmaceutical compositions comprising a ligand protein complexed with a soluble receptor protein are provided. In certain embodiments, the ligand is selected from the group consisting of interleukins, colony stimulating factors, and tumor necrosis factor.

(FILE 'HOME' ENTERED AT 12:38:33 ON 08 SEP 2000)

FILE 'MEDLINE, EMBASE, SCISEARCH, USPATFULL, BIOSIS' ENTERED AT 12:39:09
ON 08 SEP 2000

```
L1         20892 S (ANTIBOD? OR PROTEIN? OR MACROMOLECUL?) (3A) (INJECT?)
L2        203489 S (BIND? OR CAPTUR? OR TARGET?) (5P) (IN VIVO)
L3          2748 S L1 (5A) L2
L4          1123 S (ANTIBOD? OR PROTEIN? OR MACROMOLECUL?) (5A) (INJECT?) (5A)
(
L5         29815 S (BIND? OR CAPTUR? OR TARGET?) (5A) (IN VIVO)
L6           150 S L4 AND L5
L7           120 DUP REM L6 (30 DUPLICATES REMOVED)
L8            91 S L7 AND ?ASSAY?
L9         21109 S (INJECT?) (2A) (ANTIGEN? OR ANTIBOD? OR PROTEIN? OR
MACROMOLE
L10          552 S L9 AND L5
L11          388 S L10 AND ?ASSAY?
L12          384 DUP REM L11 (4 DUPLICATES REMOVED)
L13           20 S L9 (5A) L5
L14            9 DUP REM L13 (11 DUPLICATES REMOVED)
L15          153 S L10 AND (CYTOKINE? OR LYMPHOKINE? OR LYMPHOTOXIN? OR
INTERKEU
L16          148 S L15 AND ?ASSAY?
L17           62 S L16 AND (SANDWICH OR IMMUNOMETRIC)
L18           62 DUP REM L17 (0 DUPLICATES REMOVED)
L19        14986 S (BIND? OR CAPTUR? OR TARGET?) (2A) (IN VIVO)
L20            3 S L19 (5A) L9
L21           74 S L19 (P) L9
L22          112 S L19 (3P) L9
L23           43 S L22 AND ?ASSAY?
L24           39 DUP REM L23 (4 DUPLICATES REMOVED)
L25           13 S L24 AND L15
L26           13 DUP REM L25 (0 DUPLICATES REMOVED)
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L24 ANSWER 37 OF 39 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 85289488 MEDLINE
DOCUMENT NUMBER: 85289488
TITLE: Characterization of the binding properties and retrograde axonal transport of a monoclonal antibody directed against the rat nerve growth factor receptor.
AUTHOR: Taniuchi M; Johnson E M Jr
CONTRACT NUMBER: GM-07200 (NIGMS)
5-T32-GM07805 (NIGMS)
SOURCE: JOURNAL OF CELL BIOLOGY, (1985 Sep) 101 (3) 1100-6.
Journal code: HMV. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198512

AB We have demonstrated in vitro and in **vivo** the specific **binding** of a monoclonal antibody to the rat nerve growth factor (NGF) receptor. Previous work had shown that this antibody, designated 192-IgG, does not compete with NGF for binding to the NGF receptor of PC12 cells, but instead interacts with the receptor to increase NGF binding to PC12 cells (Chandler, C. E., L. M. Parsons, M. Hosang, and E. M. Shooter, 1984, J. Biol. Chem., 259:6882-6889). In the present study, a solid-phase separation **assay** verified the specific formation of a ternary complex of 192-IgG, the NGF receptor, and NGF: 125I-labeled 192-IgG precipitated from solution only when incubated with both solubilized NGF receptor and NGF covalently linked to a solid phase (Sepharose 4B). Filtration **assays** using plasma membrane preparations of various tissues showed strict correlation of 125I-192-IgG and 125I-labeled NGF binding; only membranes obtained from superior cervical ganglion bound significant amounts of the monoclonal **antibody** and NGF. **Injection** of 125I-192-IgG into the rat anterior eye chamber led to accumulation of intact antibody molecules in the ipsilateral superior cervical ganglion, indicating retrograde axonal transport of 125I-192-IgG from the neuronal termini, located at the iris, to the cell bodies situated in the ganglion. The time course and saturation characteristics of 125I-192-IgG retrograde transport were very similar to those previously reported for 125I-NGF transport, indicating that 192-IgG can be internalized and transported by the same mechanisms as is NGF. Consistent with results of the in vitro binding **assays**, 192-IgG and NGF failed to compete for retrograde transport and were actually co-transported. Retrograde axonal transport of 192-IgG appears to be species specific, since 125I-192-IgG was transported in the rat, but not in mice, gerbils, hamsters, or guinea pigs. These results establish monoclonal antibody 192-IgG as a specific probe for the rat NGF receptor in vitro and in vivo.

AB We have demonstrated in vitro and in **vivo** the specific **binding** of a monoclonal antibody to the rat nerve growth factor (NGF) receptor. Previous work had shown that this antibody, designated.

. M. Parsons, M. Hosang, and E. M. Shooter, 1984, J. Biol. Chem., 259:6882-6889). In the present study, a solid-phase separation **assay** verified the specific formation of a ternary complex of 192-IgG, the NGF receptor, and NGF: 125I-labeled 192-IgG precipitated from solution only when incubated with both solubilized NGF receptor and NGF

L24 ANSWER 30 OF 39 USPATFULL
ACCESSION NUMBER: 91:75520 USPATFULL
TITLE: Method for selection of primate tumor-associated antigens suitable as in vivo targets for antibodies
INVENTOR(S): Ballou, Byron T., Pittsburgh, PA, United States
PATENT ASSIGNEE(S): University of Pittsburgh, Pittsburgh, PA, United States
(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5049373	19910917
APPLICATION INFO.:	US 1990-533166	19900713 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 1989-295775, filed on 11 Jan 1989, now patented, Pat. No. US 4978520 which is a continuation-in-part of Ser. No. US 1986-906161, filed on 11 Sep 1986, now patented, Pat. No. US 4798719
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Maples, John S.
LEGAL REPRESENTATIVE: Reed Smith Shaw & McClay
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 383
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is a process for the selection of antigens which are suitable **targets** for in **vivo** antibody localization in human tumors or other altered (or diseased) tissue. The process provides a simplified and rapid technique for discovering useful in **vivo targets** for antibodies and is useful in cancer detection and therapy in humans or other primates, whether or not the antigens are specific to tumors. More specifically, the invention relates to a process for the selection of antigens suitable as targets for antibodies which localize in a tumor in vivo in which antibodies are first prepared distinguishable from those present in the animal in which biofiltration is to occur and that bind to antigens present in the tumor to be targeted. These **antibodies** are then **injected** into a non-tumor-bearing primate, into a tumor-bearing animal, and into a non-tumor bearing animal of the same species as the tumor-bearing animal to permit biofiltration of the antibodies. The biofiltered antibodies are next recovered from each of the non-tumor-bearing primate, the tumor-bearing animal, and the non-tumor-bearing animal and are employed to identify antigens whose antibodies are not retained in vivo in the primate and the non-tumor-bearing animal. The antibodies that are not retained in vivo by the non-tumor-bearing primate and the non-tumor bearing animal are then compared with those antibodies that are actually retained in vivo in the tumor-bearing animal to identify the antigens corresponding to those antibodies that are selectively retained in the tumor-bearing animal. In an alternative process, the tumor-bearing animal may be replaced by a perfusable surgically removed human organ bearing a tumor, and the non-tumor-bearing animal may be replaced by a surgically removed normal organ. Passage through a primate, however, remains the method of choice for selecting antigens

whose antibodies are unabsorbed in vivo.

AB The present invention is a process for the selection of antigens which are suitable **targets** for in **vivo** antibody localization in human tumors or other altered (or diseased) tissue. The process provides a simplified and rapid technique for discovering useful in **vivo targets** for antibodies and is useful in cancer detection and therapy in humans or other primates, whether or not the antigens. . . animal in which biofiltration is to occur and that bind to antigens present in the tumor to be targeted. These **antibodies** are then **injected** into a non-tumor-bearing primate, into a tumor-bearing animal, and into a non-tumor bearing animal of the same species as the. . .

SUMM . . . prepared by selecting monoclonal antibodies that are more highly bound to tumors than to normal tissues in in vitro screening **assays**. The present invention is for a novel selection methodology, which permits analysis of a wider range of antigens than are. . .

DETD 6. Confirmation that the antibodies do define a specificity suitable for in **vivo targeting** is done by (a) selecting specific antibodies defined by biofiltration, (b) radiolabeling the selected **antibodies**, then (c) **injecting** the radiolabeled, selected antibodies into tumor-bearing animals.

L26 ANSWER 3 OF 13 USPATFULL
ACCESSION NUMBER: 2000:15317 USPATFULL
TITLE: Immunological preparation for concurrent specific binding to spatially exposed regions of vascular permeability factor bound in-vivo to a tumor associated blood vessel
INVENTOR(S): Senger, Donald R., Medfield, MA, United States
Dvorak, Harold F., Newton, MA, United States
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, Boston, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6022541	20000208
APPLICATION INFO.:	US 1997-807992	19970303 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-327709, filed on 24 Oct 1994, now patented, Pat. No. US 5659013, issued on 19 Aug 1999 which is a continuation of Ser. No. US 1991-779384, filed on 18 Oct 1991, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Saunders, David
ASSISTANT EXAMINER: VanderVegt, F. Pierre
LEGAL REPRESENTATIVE: Prashker, David
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 30 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 2130
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides an immunological preparation comprising not less than two types of conjugate molecules in admixture for concurrent specific binding to a spatially exposed region of vascular permeability factor (VPF) bound in-vivo to a tumor-associated blood vessel. Each conjugate molecule type comprises at least a binding portion of an antibody specific for an epitope present within a spatially exposed region of bound VPF; and an effector moiety covalently bound to the specific binding portion. The immunological preparation has wide uses and applications including analytical studies, in-vivo diagnostic testing, and in-vivo therapeutic treatments.

L26 ANSWER 4 OF 13 USPATFULL
ACCESSION NUMBER: 1999:141911 USPATFULL
TITLE: Genetic induction of receptors for targeted radiotherapy
INVENTOR(S): Buchsbaum, Donald J., Birmingham, AL, United States
Raben, David, Englewood, AL, United States
Khazaeli, Mohammad B., Birmingham, AL, United States
Curiel, David T., Birmingham, AL, United States
Stackhouse, Murray, Helena, AL, United States
PATENT ASSIGNEE(S): UAB Research Foundation, Birmingham, AL, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5981504	19991109
APPLICATION INFO.:	US 1997-948132	19971009 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-739826, filed

on 11 Feb 1997
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Campbell, Bruce R.
LEGAL REPRESENTATIVE: Adler, Benjamin Aaron
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 34 Drawing Page(s)
LINE COUNT: 2609
AB The present invention provides a method to achieve radioisotopic localization at tumor sites, i.e., a method of enhancing radiolabeled ligand localization to a tumor in an individual in need of such treatment, comprising the steps of: transducing said tumor with a gene encoding a membrane expressed protein unique to said tumor; and administering to said individual a radiolabeled ligand which specifically binds to said protein. The use of gene therapy technology to induce expression of high affinity membrane molecules/receptors can enhance the specificity of radioisotope localization while the use of radioactive isotopes with the ability to deliver radiation damage across several cell diameters will compensate for less than perfect transduction efficiency.

L26 ANSWER 3 OF 13 USPATFULL
DETD . . . regions of the VPF bound in-vivo--so long as each epitope and each region remains spatially exposed and topographically available after **binding** in-**vivo**. The user may then chose which exposed epitopes and which spatially available regions are most suitable and desirable in order. . .

DETD . . . in-vivo to specific receptors on the surface of the endothelium of a tumor-associated blood vessel, one direct consequence of such in-**vivo binding** is a marked reduction and loss of external surface area and exposed topographical features for the VPF molecule in-situ. Thus,. . .

DETD . . . bound only to those amino acid sequences selectively. (b) Only three regional antibodies of the ten prepared were able to **bind** specifically to VPF under in-**vivo** conditions. This revealed that the other seven regions were either spatially obstructed or topographically internalized within the overall three-dimensional structure. . . and a limited number of amino acid residues were available as antigenic determinants in the 189 length VPF molecule after **binding** in-**vivo** to the endothelial cells.

DETD . . . spatially exposed regions of VPF bound in-vivo. It is therefore deemed conventional and expected that a wide variety of different **immunoassay** systems may be employed to demonstrate the specific binding capability required by the conjugate molecules of the present invention; and. . . antibody fragments and subunits employed for this purpose. The present invention therefore presumes and incorporates by reference any conventionally known **immunoassay** technique, procedure, protocol, or other non-decisive factor or parameter--all of which may be usefully employed for the evaluation and/or preparation.

.

DETD . . . effector moieties which injure, damage, disrupt or negatively affect the endothelial cell in-vivo. The choices not only include bacterial exotoxins, **cytokines**, enzymes, active complexes, heavy metals, and specific antimetabolites. Rather, the effector moiety may also take form as a radionuclide having. . .

DETD . . . Exotoxins (modified)

cholera toxin;
ricin;
shigella entero toxin
pertusis toxin;
tetanus toxin; - pseudonomos toxin;
diptheria toxin fragments;
staphylococcus enterotoxin.

B. **Cytokines**

lymphotoxins (LT);
tumor necrosis factor alpha (TNF-a);
interleukins (IL-2, 4, 6, 8 or 10);
interferons (alpha, beta, gamma).

C. Enzymes

deaminoses; (. . .

DETD Antibody absorption of VPF and Miles vessel permeability **assay**

.

DETD . . . Cancer Res. 50: 1774-1778 (1990)]. Adsorbed supernatants and other samples were tested for VPF activity in the Miles vessel permeability **assay** on depilated, adult Hartley guinea pigs

following i.v. injection of Evans blue dye [Senger et al., Science 219: 983-985 (1983);. . . by incubating VPF with different concentrations of antibodies at room temperature for 30 min prior to testing in the Miles **assay**. VPF adsorption and initial assessments of VPF permeability blocking activity by antibodies were graded by estimating the intensity of the. . .

DETD . . . reacted against the respective immunizing peptides. Antisera also were tested for reactivity with VPF on immunoblots and in an immunoadsorption **assay**. Immunoblots were performed on reduced human or guinea pig VPF and similar results were obtained with both, although a relatively. . .

DETD . . . protein A-Sepharose and used to adsorb native VPF from solution. The unbound VPF was detected with the Miles vessel permeability **assay**.

DETD . . . antibody was adsorbed onto protein A-Sepharose and was incubated with VPF at dilutions suitable for testing in the Miles permeability **assay**. Supernatants remaining after removal of the VPF-antibody-bound beads by centrifugation were tested for residual VPF activity and scored against VPF. . .

DETD . . . of VPF then were tested for their ability to diminish VPF activity when coinjected with VPF in the Miles permeability **assay**. Because guinea pigs may express hypersensitivity to whole rabbit sera, antibodies were affinity-purified before testing.

DETD . . . that from sites injected with VPF alone. % block of permeability is expressed as mean .+-.SE for each amount of **antibody** per **injection**.

DETD . . . measured separately to assess free and cell-bound antibody. Drinking water was supplemented with 0.1% w/v NaI beginning 24 h before **injecting** radiolabeled **antibodies**. At least 3 animals (4-6 tumors) were studied at each time point for each antibody. Analysis of variance and statistical. . .

DETD . . . of its epitopes are no longer spatially accessible to antibody; in comparison, epitopes associated with VPF's N-terminus retained their capacity in-**vivo** to **bind** specific antibodies after becoming bound to and associated with microvessel endothelium. It is concluded also that the pool of free. . .

DETD Avidin-peroxidase staining for tissue localization of i.v. **injected** biotinylated **antibodies**

DETD The distribution of biotinylated Ab-VPF-N and control antibodies was followed in solid- or ascites tumor-bearing mice. 100 .mu.g of biotinylated **antibodies** were **injected** i.v. in 200 .mu.l of 0.1% BSA-normal saline. Twenty-four hours later, solid tumor-bearing mice were killed and exsanguinated; ascites tumor-bearing. . .

DETD Localization of i.v. **injected** biotinylated **antibodies** in tumor-associated microvessels

DETD Biotinylated Ab-VPF-N (bAb-VPF-N) or rRIgG (b-nRLgG) **antibodies** were **injected** i.v. into mice bearing either ascites or solid MOT tumors; and were distributed in peritoneal lining tissues of ascites tumor. . .

L26 ANSWER 4 OF 13 USPATFULL

SUMM . . . use of various radionuclides (5), the use of more stable (26) or enzymatically cleavable chelating agents (27), the use of **cytokines** to upregulate tumor-associated antigen expression (28, 29), irradiation of the tumor to increase vascular permeability (14, 30-32), the use of **cytokines** to protect against bone marrow suppression (33, 34), and the use of autologous bone marrow transplantation (2, 35). Despite these. . .

DRWD . . . in D54 MG human glioma cells transfected in vitro with AdCMVCEA or AdCMVLacZ at 1 PFU/cell or mock-infected. Cells were **assayed** 48 hours post-transfection. The photographs shown depict: (FIG. 3A) D54 MG cells/AdCMVCEA, (FIG. 3B) D54 MG cells/AdCMVLacZ, (FIG. 3C) D54. . .

DRWD . . . of .sup.125 I-labeled COL-1 MAb to AdCMVCEA transduced D54 MG cells. D54 MG cells were transfected with 1 PFU-cell and **assayed** 48 hours post-transfection. Both control virus (AdCMVLacZ) and control antibody (CC49) as well as non-transduced D54 MG cells were analyzed. .

DRWD FIG. 6 shows the analysis of binding activity of .sup.125 I-labeled COL-1 MAb to AdCMVCEA transduced D54 MG cells **assayed** at varying days post-transfection. The histogram depicts the molecules of COL-1 bound/cell at 2, 9, and 13 days post-transfection in. . .

DRWD . . .) pfu/cell AdCMVGRPr or 100 pfulcell ACMVLacZ ( ). Fourty-eight hours following infection, cells were harvested for a live-cell binding **assay** with [125I]-Tyr4-bombesin and compared to the mouse fibroblast BNR-11 cells that stably express mGRPr. In FIGS. 21A and B, (. . .

DETD . . . transducibility, cells were harvested 48 hours post-transduction, lysed, and analyzed for luciferase expression as described by the manufacturer (Promega Luciferase **Assay** System, Madison, Wis.). Briefly, lysates from transfected cells were obtained after removal of the tissue culture media and adding 150. . . centrifugation at 13,000.times. g for 3 minutes. The cell extract (20 .mu.l) was then added to 100 .mu.l of luciferase **assay** reagent and analyzed for emitted light in a Lumat LB9501 luminometer (Berthold Systems Inc., Aliquipa, Pa.).

DETD . . . cDNA construct (141). Large scale preparation of the CEA encoding virus, AdCMVCEA, was accomplished and purified virus titered by plaque **assay** techniques for direct determination of viral PFU employing 293 cells as the target.

DETD . . . AdCMVLacZ vector at either 1 or 10 PFU/cell. Two-days post-injection, cells were analyzed for CEA expression via an indirect immunofluorescence **assay**, a radiolabeled binding **assay** , and by immunohistochemistry, as described below. As a positive control, the LS174T human adenocarcinoma, known to constituitively express CEA, was. . .

DETD . . . Piscataway, N.J.). Specific activities of radiolabeled preparations were determined. Immunoreactivity of radiolabeled antibody preparations was measured using a live cell-binding **assay** with LS174T cells for COL-1 and SW1116 cells prepared from tumor xenografts for CC49 using the Lindmo method as described. . .

DETD A radiolabeled antibody binding **assay** was performed to analyze CEA cell surface expression. Binding activity of .sup.125 I-labeled COL-1 or CC49 antibody preparations were measured using an in vitro live

cell-binding **assay**. AdCMVCEA or AdCMVLacZ transfected D54 MG human glioma cells were harvested using 4 mM EDTA, 0.05% KCl in PBS, pH.

. .

DETD To demonstrate that one could augment radiolabeled antibody **targeting** in **vivo**, D54 MG cells were initially transduced in vitro with AdCMVCEA or AdCMVLacZ at 1 PFU/cell. After 2 days in culture,. . .

DETD . . . previously shown to localize in LS174T tumor xenografts (4,151,153). For this analysis, 100 or 300 .mu.Ci of .sup.131 I-labeled COL-1 **antibody** were **injected** intraperitoneally into groups of mice bearing established tumors of 5-10 mm in diameter. Thyroid uptake was blocked by adding a. . . to their drinking water. Whole body scans of anesthetized (100 mg/kg sodium pentobarbital) mice were obtained 5 days after radiolabeled **antibody** **injection** using a large field-of-view Sopha DSX camera (Sopha Medical, Columbia, Md.) fitted with a 4 mm pinhole collimator interfaced to. . . of liver, kidney, spleen, lung, small intestine, femur, skin, muscle, tumor, and blood were blotted dry, weighed, and the radioactivity **assayed** in a well-type gamma counter (Minaxi-gamma 5000 series, Packard, Chicago, Ill.) to determine the tissue distribution of .sup.131 I-labeled COL-. . .

DETD . . . MG cells transfected with AdCMVLacZ at 1 or 10 PFU/cell served as negative controls. Two-days post-transfection cell membrane-associated CEA was **assayed** with anti-CEA MAb COL-1 or with CC49, a negative control antibody. The LS174T human adenocarcinoma cells, known to constitutively express. . .

DETD Experiments were then conducted using an in vitro live cell radiolabeled antibody binding **assay** to quantify the level of CEA expression in AdCMVCEA transduced D54 MG cells. These results indicated high binding efficiency of. . .

DETD . . . gene expression (4), the persistence of cell surface CEA expression in AdCMVCEA transduced D54 MG cells was determined. Radiolabeled binding **assays** were performed at 2, 9, and 13 days post-transfection with AdCMVCEA at 1 PFU/cell. .sup.131 I-labeled COL-1 binding to CEA. . .

DETD . . . PFU AdCMVCEA 2 days before intraperitoneal injection of 100 .mu.Ci .sup.131 I-labeled COL-1 was 1.5.+-.0.7 %ID/g at 4 days after **antibody injection**, which was similar to that in nontransduced D54 MG tumors in the same weight range after 1 intratumor injection of. . .

DETD . . . received two intratumoral injections of 1.times.10.sup.9 PFU AdCMVCEA 1 and 2 days before COL-1 injection, and at 2 days after **antibody injection** are shown in Table III.

DETD . . . These same cells transfected with AdCMVLacZ at 1 PFU/cell served as negative controls. Two days post-transfection cell membrane-associated CEA was **assayed** with .sup.125 I-labeled COL-1 anti-CEA MAb. The results indicated high binding efficiency of radiolabeled anti-CEA antibody to Calu-3 and A427. . .

DETD . . . cell lines can be transduced using AdpL transfection. The genetic constructs developed are validated using AdpL transfection and the appropriate **assay** for gene expression. The next step to develop GRITS in breast cancer cells was to demonstrate CEA induction after infection. . .

DETD . . . a Stratagene Robocycler with a temperature gradient. This promoter region was shown to have tissue specific expression using a CAT **assay** in MCF-7 breast cancer cells (Abe and Kufe, 1993, PNAS 90:282). The upstream primer 5'GGCGGCCGCTCCTGGCCAGTGGTGGAG3' (SEQ ID No.1) contained a. . .

DETD . . . 24 hours incubation the media was removed and replaced with fresh growth media. Twenty four hours later the cells were **assayed** for expression of the firefly luciferase enzyme. A

firefly lucifase reporter **assay** kit (Promega) was used. Cells were lysed in 300 ml lysis buffer. 20 ml of sample was added to 100 ml of luciferase **assay** buffer. Luciferase expression was determined as relative light units (RLU) measured in a luminometer (10 s

counts triplicate samples). Soluble. . .

DETD . . . immunohistochemical analysis indicated substantial binding of unlabeled COL-1 to AdCMVCEA transduced D54 MG cells maintained in culture. Furthermore, radiolabeled binding **assays** confirmed the ability of AdCMVCEA to transduce D54 MG cells to express CEA as the data revealed impressive .sup.125 I-labeled. . .

DETD . . . high levels of induced peptide binding, with approximately 60-80% of the radioactivity bound to the cells, in a live-cell binding **assay**. The human ovarian carcinoma cell line SKOV3.ip1 was chosen for in vivo analysis of radiolabeled bombesin analogue tumor localization in. . .

DETD . . . of tumor types. Additionally, a well characterized murine model

of human ovarian carcinoma was genetically induced to express mGRPr in **vivo** to **target** the tumor with the radiolabeled bombesin analogue. The biodistribution and pharmacokinetics of the radiolabeled bombesin analogue were analyzed in tumor. . .

DETD . . . control for analysis of genomic DNA derived from AdCMVGRPr. Adenoviral vectors were titered within the cell line 293, employing plaque **assay** techniques for direct determination of viral pfu.

DETD In vitro radiolabeled binding **assay**

DETD Infections with recombinant adenoviruses were performed as previously described. Cells were harvested for radiolabeled binding **assay** 48 hours following adenoviral mediated infection by removal at 37.degree. C. with 4 mM EDTA, 0.05% KCl. Detached cells were. . . Gaithersburg, Md.). The e21 antibody was .sup.125 I-labeled using the lodogen method and utilized in an in vitro live-cell binding **assay** with the SKOV3.ip1 cells. Cells were harvested as described above and incubated for 1 hour with 100 .mu.l of a. . .

DETD . . . I-labeled e21. Mice were sacrificed at 5 minutes, 1 and 12 hours, and 1, 2, 4 and 6 days following **antibody injection** (n=6/group). Tumor and normal organs were dissected and analyzed as described above.

DETD Live-cell binding **assays** illustrated the ability of each transfected cell line to bind an [.sup.125 I]-Tyr-bombesin peptide (FIG.

21A and 21B). The non-small. . .

DETD . . . The human ovarian carcinoma cell line SKOV3.ip1 is known to overexpress erbB-2 and was therefore utilized in a live-cell binding **assay**. Incubation of the SKOV3.ip1 cells with .sup.125 I-labeled e21 resulted in 96.3% of the total radioactivity bound to the cells. .

.

DETD . . . against the administered antibody. In an effort to overcome the

low level antigen expression problem, the utility of systemically administered **cytokines** for upregulating the expression of tumor-associated antigens, which has resulted in increased localization of radiolabeled antibodies in both animal models. . .

DETD . . . GRPr (FIG. 25B) while .sup.125 I-bombesin did (data not shown).

The use of membrane preparations has been a more sensitive **assay** than the use of live cells due to the lower background binding to the

L14 ANSWER 4 OF 9 MEDLINE
ACCESSION NUMBER: 95254598 MEDLINE
DOCUMENT NUMBER: 95254598
TITLE: Use of technetium antigranulocyte monoclonal antibody Fab' fragments for the detection of osteomyelitis.
AUTHOR: Harwood S J; Camblin J G; Hakki S; Morrissey M A; Laven D L; Zangara L M; Patel J U; Webster W B Jr; Carroll R G
CORPORATE SOURCE: Nuclear Medicine Service; Dept. of Veterans Affairs VAMC, Bay Pines, FL 33504..
SOURCE: CELL BIOPHYSICS, (1994) 24-25 99-107.
Journal code: CQC. ISSN: 0163-4992.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
AB Accurate early diagnosis of osteomyelitis is critical for optimal clinical management. Conventional radiology (X-rays, CT) and nuclear medicine scans (bone, gallium, and technetium/indium white blood cell [WBC]) have limitations and drawbacks. The monoclonal antibody (MAb) ImmuRAID-MN3 (Immunomedics Inc., Morris Plains, NJ), a 99m-Tc Antigranulocyte Fab' fragment, recognizes a surface glycoprotein NCA-90/95 shared by granulocytes, carcino-embryonic antigen (CEA), and meconium **antigen** (MA). Intravenous **injection** of radiolabeled MAb enables in **vivo** labeling of human granulocytes and **targets** infected lesions in the bone and throughout the body. Technetium labeled Fab' fragments rapidly clear the blood pool and high-quality images can be obtained the same day, as early as 1 h postinjection. Results at our institution on 13 patients with clinically suspected osteomyelitis of infected long bones, prostheses, and diabetic foot ulcers were compared with the surgical/bacteriological verification of the presence or absence of infection. The MAb scan showed six true positives, six true negatives, and one false negative (very low grade infection). The procedure was safe, no clinical or laboratory adverse reactions were encountered. The MAb fragments are markedly less immunogenic than whole IgG, resulting in lower induction of human antimouse antibody (HAMA) titers. No HAMA to this MAb fragment has been detected in 24 patients (data from multiple institutions). Our preliminary results suggest that 99m-Tc ImmuRAID-MN3 is highly accurate for detection of osteomyelitis. This study is part of an ongoing multiinstitutional project sponsored by Immunomedics, Inc. to evaluate the efficacy and safety of this radiopharmaceutical.
AB . . . Plains, NJ), a 99m-Tc Antigranulocyte Fab' fragment, recognizes a surface glycoprotein NCA-90/95 shared by granulocytes, carcino-embryonic antigen (CEA), and meconium **antigen** (MA). Intravenous **injection** of radiolabeled MAb enables in **vivo** labeling of human granulocytes and **targets** infected lesions in the bone and throughout the body. Technetium labeled Fab' fragments rapidly clear the blood pool and high-quality. . .

L14 ANSWER 5 OF 9 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 93204411 MEDLINE
DOCUMENT NUMBER: 93204411
TITLE: Binding of bacterial adhesins to rat glomerular mesangium

in vivo.

AUTHOR: Miettinen A; Westerlund B; Tarkkanen A M; Tornroth T; Ljungberg P; Renkonen O V; Korhonen T K
CORPORATE SOURCE: Department of Bacteriology and Immunology, University of Helsinki, Finland.
SOURCE: KIDNEY INTERNATIONAL, (1993 Mar) 43 (3) 592-600.
Journal code: KVB. ISSN: 0085-2538.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
AB Two well characterized bacterial adhesins, the O75X fimbriae of Escherichia coli and the type-3 fimbriae of Klebsiellae, with in vitro affinities to type IV and V collagens, respectively, were used to test whether bacterial components with affinity for glomerular matrix could **bind** to glomeruli in **vivo**. The purified fimbrial **proteins** were **injected** into rats, and kidney samples were studied by immunofluorescence at two hours to nine months postinjection. The O75X, but not the type-3 fimbriae, formed mesangial deposits that persisted for months. Preincubation of the O75X fimbriae with type IV collagen significantly reduced the glomerular binding. The fimbrial deposits were extracellular, as anti-O75X IgG injected into rats bound to glomeruli. Proteinuria or histological damage could not be detected even after passive or active immunizations of the rats. The results demonstrate that bacterial adhesins may bind in vivo to and persist in glomeruli by their specific affinities. The results also indicate that additional factors provided by the bacteria or the host are needed for glomerular damage to take place.
AB . . . to type IV and V collagens, respectively, were used to test whether bacterial components with affinity for glomerular matrix could **bind** to glomeruli in **vivo**. The purified fimbrial **proteins** were **injected** into rats, and kidney samples were studied by immunofluorescence at two hours to nine months postinjection. The O75X, but not. . .

L14 ANSWER 7 OF 9 MEDLINE
ACCESSION NUMBER: 89092552 MEDLINE
DOCUMENT NUMBER: 89092552
TITLE: Localization of biotinylated monoclonal antibody in nude mice bearing subcutaneous and intraperitoneal human tumour xenografts.
AUTHOR: Pervez S; Paganelli G; Epenetos A A; Mooi W J; Evans D J; Krausz T
CORPORATE SOURCE: Department of Histopathology, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK..
SOURCE: INTERNATIONAL JOURNAL OF CANCER. SUPPLEMENT, (1988) 3 30-3.
Journal code: GRM. ISSN: 0020-7136.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198904
AB To demonstrate the precise distribution and **binding** of in **vivo injected** monoclonal **antibodies** on histological tumour sections, we have biotinylated our primary antibody AUA1. Biotinylated antibody was injected into nude mice bearing simultaneous subcutaneous and intraperitoneal xenografts of the human tumour LoVo. Twenty-four hours after injection, the animals were killed, tumours and control organs were removed. Antibody was demonstrated on frozen sections by incubating sections with avidin biotin peroxidase complex. We compared the in vivo penetration and binding of this antibody on intraperitoneal and subcutaneous xenografts. The antibody penetration was mainly restricted to a thin layer of tumour cells adjacent to the vascularized stroma in large solid subcutaneous and intraperitoneal tumours, whereas in very small intraperitoneal tumours, antibody penetration was complete. These findings were similar to our autoradiographic results. This study demonstrates that employing the biotinylated antibodies for in vivo localization studies provides superior resolution of antibody binding for morphological assessment compared to autoradiography. Localization of a biotin label is more precise and will permit ultra-structural studies.
AB To demonstrate the precise distribution and **binding** of in **vivo injected** monoclonal **antibodies** on histological tumour sections, we have biotinylated our primary antibody AUA1. Biotinylated antibody was injected into nude mice bearing simultaneous. . .

covalently linked to a solid phase (Sepharose 4B). Filtration **assays** using plasma membrane preparations of various tissues showed strict correlation of 125I-192-IgG and 125I-labeled NGF binding; only membranes obtained from superior cervical ganglion bound significant amounts of the monoclonal **antibody** and NGF. **Injection** of 125I-192-IgG into the rat anterior eye chamber led to accumulation of intact antibody molecules in the ipsilateral superior cervical. . .
can
be internalized and transported by the same mechanisms as is NGF. Consistent with results of the in vitro binding **assays**, 192-IgG and NGF failed to compete for retrograde transport and were actually co-transported. Retrograde axonal transport of 192-IgG appears to. . .

L24 ANSWER 39 OF 39 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 79172334 MEDLINE
DOCUMENT NUMBER: 79172334
TITLE: Murine natural anti-tumor antibodies. I. Rapid in vivo binding of natural antibody by tumor cells in syngeneic mice.
AUTHOR: Wolosin L B; Greenberg A H
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (1979 Apr 15) 23 (4) 519-29.
Journal code: GQU. ISSN: 0020-7136.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197909
AB A competitive **radioimmunoassay** (RIA) for the detection of cell-bound antibody was used to study the in vivo acquisition of immunoglobulin (Ig) by tumor cells. Several tumor lines acquired Ig rapidly between 3 and 18 h after intraperitoneal implantation into normal syngeneic mice and this Ig was recovered by elution with basic or acid buffers. The Ig eluted from the L5178Y lymphoma showed higher binding to the L5178Y than to thymocytes, bone-marrow cells, 1509a sarcoma and P-815-X2 mastocytoma. In addition, binding of the eluates to the L5178Y was specifically inhibited by L5178Y cells or by solubilized membrane antigens of the L5178Y. The in vivo acquisition of Ig by the L5178Y could also be blocked by the IV and IP **injections** of tumor **antigen** although both L5178Y and 1509a solubilized membrane antigens were effective. Some of the Ig acquired by the tumor cells was found to be complement-fixing antibody since normal rabbit complement lysed 80% of L5178Y cells obtained from the peritoneal cavity of
syngeneic
mice 18 h after implantation, but did not lyse in vitro L5178Y cells. The in **vivo binding** of the complement-fixing antibodies was also inhibited by tumor antigens in the same way as the acquisition
of
Ig detected by RIA. It was shown that the acquisition of Ig during the first 18h of IP growth was a T-independent phenomenon because tumor cells acquire as much Ig in AT X BM mice as in sham-thymectomized controls. In
a
study with 11 different clones derived from the L5178Y lymphoma, a high correlation (r = 0.75, p less than 0.005) was found between the amount of Ig acquired after in vivo implantation and the amount of Ig bound to the cells after in vitro incubation with normal syngeneic serum. It is suggested that the rapid in vivo acquisition of Ig was due to the in **vivo binding** of natural antibodies to tumor cells.
AB A competitive **radioimmunoassay** (RIA) for the detection of cell-bound antibody was used to study the in vivo acquisition of immunoglobulin (Ig) by tumor. . . the L5178Y. The in vivo acquisition of Ig by the L5178Y could also be blocked by the IV and IP **injections** of tumor **antigen** although both L5178Y and 1509a solubilized membrane antigens were effective. Some of the Ig acquired by the tumor cells was. . . the peritoneal cavity of
syngeneic

mice 18 h after implantation, but did not lyse in vitro L5178Y cells. The in **vivo binding** of the complement-fixing antibodies was also inhibited by tumor antigens in the same way as the acquisition of Ig detected. . . with normal syngeneic serum. It is suggested that the rapid in vivo acquisition of Ig was due to the in **vivo binding** of natural antibodies to tumor cells.

CT . . .
IgG

Immune Sera
Immunoglobulins, Fc
Immunoglobulins, Surface
Lymphoma: IM, immunology
Mice
Mice, Inbred Strains
Neoplasm Transplantation
*Neoplasms, Experimental: IM, immunology
Radioimmunoassay
Thymectomy
Transplantation, Isogeneic

and produce immunogenic hapten-carrier conjugates. In contrast to previous studies in which hapten-carrier conjugates have been generated following chemical modification of drugs we have examined the immunogenicity of paracetamol following direct conjugation to carrier **proteins** with horseradish peroxidase (HRP). Highly substituted conjugates of paracetamol with keyhole limpet haemocyanin (KLH) or bovine serum albumin (BSA) were generated using HRP. The KLH conjugated was used to immunize Balb/C mice. IgM and IgG (predominantly IgG1) responses were observed and shown by enzyme-linked immunosorbent assay (ELISA) to be hapten-specific. Manipulations of HRP levels permitted substitution of KLH to varying extents with paracetamol. Such conjugates were tested for their ability to induce a hapten-specific immune response. It was determined that substitution of 1 mol of KLH with 700 mol of paracetamol was sufficient to generate an **anti-hapten** response. These data suggest a mechanism by which **protein**-non-reactive drugs may be rendered immunogenic and provide a method for demonstrating the presence of serum antibodies reactive with drug metabolites.